IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant:	William Malcolm Charles Rosenberg		
Application No.:	10/501,262	Group:	1637
Filed (371(c)):	February 5, 2005	Examiner:	Angela Marie Bertagna
Confirmation No.:	3832		

For: Methods of Detecting HCV Genotype 1 (HCV-1) by Using Primers Specific for the 5' Non-Coding Region (NCR) of the HCV Genome

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REPLY TO RESTRICTION REQUIREMENT AND PRELIMINARY AMENDMENT

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Responsive to the Restriction Requirement dated February 14, 2007, the claims of Group II (Claims 16, 18-20, and 22-30), drawn to oligonucleotides (primers, probes), and kits comprising oligonucleotides, are elected for prosecution. Applicant reserves the right to file a continuing application or take such other appropriate action as deemed necessary to protect the non-elected inventions. Applicant does not hereby abandon or waive any rights in the non-elected inventions.

An extension of time to respond to the Restriction Requirement is respectfully requested. A Petition for an Extension of Time and the appropriate fee are being filed concurrently.

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01 FC:1253 1020.00 OP
02 FC:1201 200.00 OP
03 FC:1202 350.00 OP

In addition to an election of a group of claims, the Examiner has further required election of a conserved primer pair for examination. Applicant elects the primer pair of SEQ ID NO:2 and SEQ ID NO:3.

The Examiner has also required that Applicant "select a reverse primer from SEQ ID NO:1 and SEQ ID NO:2 for examination." Applicant notes that the oligonucleotides designated SEQ ID NO:2 and SEQ ID NO:5 are reverse primers; the oligonucleotides designated SEQ ID NO:1 and SEQ ID NO:7 are specific primers that hybridize specifically to the HCV-1 5' noncoding region, but not to the nucleic acid of other HCV genotypes. If the Examiner intended Applicant to select a *reverse* primer from between SEQ ID NO:2 and SEQ ID NO:5, Applicant selects 5. If the Examiner intended Applicant to select a *specific* primer from between SEQ ID NO:1 and SEQ ID NO:7, Applicant selects SEQ ID NO:1. If the Examiner intended a selection between SEQ ID NO:1 and SEQ ID NO:2, Applicant selects SEQ ID NO:1.

Applicant notes that the Examiner will examine the specific primer of SEQ ID NO:7 and the probe of SEQ ID NO:6 in addition to the above selected sequences.

According to the Examiner's further restriction of oligonucleotides by SEQ ID NO, Claims readable on the elected primer pair SEQ ID NO:2 and SEQ ID NO:3, and the oligonucleotides SEQ ID NO:7, SEQ ID NO:6 (probe) and SEQ ID NO:1 are

(primer pair SEQ ID NO:2 and SEQ ID NO:3): 19, 23, 24, and 25;

(probe SEQ ID NO:6): 20 and 30;

(primer SEQ ID NO:7): 16, 18, 22, 23, 24, 25, 29, 30, 31, 32, 35 and 36; and if SEQ ID NO:1 is an additional option, 16, 18, 22, 23, 24, 25, 27, 29, and 30. Thus, Claims 16, 18-20, 22-25, 27, 29, 30-32, 35 and 36 are readable on the combination of SEQ ID NOs 2 and 3 (as a pair), 7, 6 and 1.

If SEQ ID NO:5 is an option in addition to the pair SEQ ID NO:2 and SEQ ID NO:3, and the oligonucleotides SEQ ID NO:6 (probe) and SEQ ID NO:7, Claims readable on this combination are 16, 18-20, 22-25, 29-32, 35 and 36.

The requirement to elect a group of claims is not traversed. However, the requirement for further restriction among primers is being traversed for the reasons set forth in detail below.

The invention is, in part, a method to detect the presence of HCV genotype 1 (HCV-1) nucleic acid in a sample, and to distinguish it from the nucleic acid of HCV of other genotypes.

Applicant has found oligonucleotides that hybridize specifically to nucleic acid of HCV-1, in the 5' noncoding region, and do not hybridize detectably by DNA amplification methods to nucleic acid of HCV of other genotypes can be used in these methods. These oligonucleotides include, in specific embodiments, the oligonucleotide comprising SEQ ID NO:1 and the oligonucleotide comprising SEQ ID NO:7. Note that SEQ ID NO:7 bears modifications to allow for fluorescent detection of amplified DNA products, but that SEQ ID NO:1 and SEQ ID NO:7 have in common 14 nucleotides at their 3' ends.

A kit to carry out the method must contain at least one oligonucleotide specific to HCV-1 (for example, either an oligonucleotide comprising SEQ ID NO:1 or an oligonucleotide comprising SEQ ID NO:7), and an oligonucleotide primer (a reverse primer) to be paired with this oligonucleotide in an amplification reaction. Either an oligonucleotide comprising SEQ ID NO:2 or an oligonucleotide comprising SEQ ID NO:5 can serve as a reverse primer, for example. If an oligonucleotide comprising SEQ ID NO:1 is used as a forward specific primer, the oligonucleotide comprising SEQ ID NO:6 can be used as a probe to detect amplification products.

It can be seen that to specifically detect HCV-1, a kit can contain, in specific embodiments, (1) the combination of the oligonucleotide comprising SEQ ID NO:7, with either SEQ ID NO:2 or SEQ ID NO:5 as a reverse primer partner in a primer pair, or (2) the oligonucleotide comprising SEQ ID NO:1, with either SEQ ID NO:2 or SEQ ID NO:5 as a reverse primer partner in a primer pair. Because SEQ ID NO:1 does not bear a fluorescent label, a means of detection of amplification products is desirable when SEQ ID NO:1 is used as a specific (forward) primer. The oligonucleotide comprising SEQ ID NO:6 can be used as a detection probe.

Further information can be gained by amplifying the nucleic acid in the sample with a universal forward primer (e.g., oligonucleotide primers comprising SEQ ID NO:3 or SEQ ID NO:4) with a universal reverse primer (e.g., oligonucleotide primers comrprising SEQ ID NO:2 or SEQ ID NO:5). In other embodiments, an oligonucleotide comprising SEQ ID NO:8 (a fluorescently labeled (beacon) forward primer) can be paired with either of the oligonucleotide primers comprising SEQ ID NO:2 or SEQ ID NO:5 (universal reverse primers). Detection of amplification products using these primer pairings indicates that HCV (any genotype) nucleic acid is present.

Thus, to provide sufficient components in a kit to specifically detect HCV-1 nucleic acid, the kit should comprise at least one pair of primers that specifically amplify HCV-1 DNA. In specific embodiments, the pair can be any of the following (oligonucleotides comprising the sequence):

SEQ ID NO:7 + SEQ ID NO:2

SEQ ID NO:7 + SEQ ID NO:5

SEQ ID NO:1 + SEQ ID NO:2

SEQ ID NO:1 + SEQ ID NO:5.

In each of these pairs, SEQ ID NO:7 or the related sequence SEQ ID NO:1 provides nucleotide sequence for specific hybridization to HCV-1. An oligonucleotide probe comprising SEQ ID NO:6 can be used to detect the products of the first two primer pairings.

The Examiner is requested to reconsider the restriction requirement described in the office action dated 14 February 2007, and to examine at least claims drawn to oligonucleotides (primers, probes, and pairs of primers) comprising SEQ ID NO:7, SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:5 or SEQ ID NO:6 so that it will be possible to obtain claims to specific embodiments of kits containing sufficient components to carry out assays described in the specification. Most important among the oligonucleotides described are those oligonucleotides that anneal specifically to the 5' noncoding region of the HCV-1 genome. Applicant therefore requests that the oligonucleotide sequences considered for examination include both SEQ ID NO:7 and SEQ ID NO:1.

Claims readable on the proposed combination of oligonucleotides are Claims 16, 18-20, 22, 27-33, and 35-37.